BUERGER'S DISEASE

Thromboangiitis obliterans or Buerger's Disease is an inflammatory condition of the small and medium-sized blood vessels of the arms and legs, leading to an insufficient supply of blood to the tissues. One of the charges against cigarette smoking is that it causes Buerger's Disease. This claim is based, in part, on reports alleging that a high percentage of patients with the disease smoke cigarettes. Despite such claims, the cause of Buerger's Disease is not yet known.[1] Moreover, problems created by frequent misdiagnoses and questions raised by the incidence or occurrence rates and other suggested theories of causation indicate that the causal hypothesis concerning Buerger's Disease and smoking is unproven.

Misdiagnosis

True Buerger's Disease is rare, even among young males in whom it reportedly occurs most frequently,[2] and misdiagnosis is common. For example, an American researcher who reviewed 205 cases diagnosed as Buerger's Disease at one hospital between 1933 and 1963 concluded that only 33 (16%) had a clinical picture compatible with the criteria for the disease.[3] One explanation for such a large number of misdiagnosed cases may be that there are many other conditions and diseases with symptoms similar to those seen in Buerger's Disease patients. These conditions and diseases, which

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include atherosclerosis (vascular blockage caused by cholesterol plaques), frostbite, gout, ergotism (poisoning from the misuse or accidental ingestion of ergot, a type of rye plant fungus used for medicinal purposes), arterial embolism, scleroderma (a skin disease), an immunological disease called periarteritis nodosa, and occupational trauma, are not generally associated with smoking in the literature. For example, atherosclerosis, one of the diseases that is often confused with Buerger's Disease, is associated with high cholesterol levels and risk factors such as hypertension and diabetes mellitus.[4] Accordingly, studies which suggest a strong association between Buerger's Disease and smoking may be flawed because it is likely that they include a number of cases in their analyses that are not actually Buerger's Disease.

Incidence of Buerger's Disease

Claims are made that the incidence of Buerger's Disease has risen and is increasing concurrently with the prevalence of smoking. However, this assertion is not consistent with the observation of a professor of medicine that "when the total number of heavy smokers in the general population is considered, the actual number in whom thromboangiitis obliterans develops is exceedingly small."[5] Furthermore, this claim is not substantiated by reports that the incidence of Buerger's Disease in women is extremely low,

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even though their smoking rates have increased dramatically in more recent years. For example, a 1973 worldwide literature review of female patients covering a period of almost 50 years reportedly found only 22 cases with microscopic findings that were compatible with those specified for the diagnosis of Buerger's Disease. Of those 22 cases, only eight were considered to be "probable" Buerger's Disease while the remainder were classified either as "possible" or only "doubtful."[6] Between 1973 and 1986, only four additional cases of the disease in women were reported in the English-speaking literature.[7] In 1986, however, a much higher incidence of Buerger's Disease was noted by an American researcher, who reported that 11 percent (12 out of 109 cases) of the patients registered with the disease at the well-known Mayo Clinic in Rochester, Minnesota, between 1981 and 1985 were women.[8] Although he speculated that the apparent rise in the incidence of the disease among U.S. women might be related to their increased use of tobacco, the incidence of the disease in these women has not risen at the same rate as their prevalence of smoking. Therefore, this does not appear to be a satisfactory explanation.

The true incidence of Buerger's Disease in the general population is difficult to determine for numerous reasons. These include the possibility that a history of smoking has been a significant source of diagnostic bias among members of the medical profession because of the assumption that a smoker who presents

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with symptoms suggestive of Buerger's Disease is more likely to have the disease than some other disease or condition with the same or similar symptoms. For example, a patient who may actually have, for example, peripheral vascular disease may be more likely to be diagnosed with Buerger's Disease largely because that individual also happens to smoke. Another reason is that the incidence rates reported in the literature are subject to certain population biases arising from the fact that most cases diagnosed as Buerger's Disease are referred to the care of health-care providers specializing in vascular diseases. Since the occurrence of the disease among such individuals or among those with peripheral vascular disease is likely to be higher than in the general population, applying those rates to the general population will likely lead to an artificially high overall rate.

There may be still other factors affecting the number of Buerger's Disease cases reported that have little to do with the true incidence of the disease. This is suggested by the dramatic changes in the reported incidence of the disease in the United States since it was first fully described by Dr. Buerger in an article in a medical journal in 1908[9] and discussed more completely in his monograph in 1924.[10] Between 1925 and 1945, one American physician claimed to have seen over 1,400 cases of Buerger's Disease, all in smokers.[11] In later years, however, the number of reported cases dropped dramatically. The reason for this drop is

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unclear, although it has been speculated that the "popularity" of the disease as a medical diagnosis declined, perhaps in part because of the medical profession's greater adherence to stricter diagnostic criteria.[12] For example, in one study at the well-known Mayo Clinic, in Rochester, Minnesota, the prevalence rate dropped from 104/100,000 registered patients in 1947 to 13/100,000 patients in 1986, even though the clinical and pathologic criteria for the diagnosis of the disease remained the same.[13]

Tobacco and Buerger's Disease

Tobacco use has been implicated in the literature as a major cause of Buerger's Disease because of its reported temporal relationship with the clinical course of the disease. That is, many have suggested that the disease will progress with the continuation of smoking and that it will not progress if tobacco use is discontinued. However, a number of researchers have reported this not to be the case. For example, in a study of Buerger's Disease in the United States Army during and after World War II, "no significant association" between smoking habits of the patients after diagnosis and subsequent amputation rates was reported.[14] Three years later, it was noted that a "careful" study of smoking habits in 81 patients with Buerger's Disease attending a British clinic "failed to find any effect of smoking on the course of the disease."[15] Similarly, in another case study of a woman with

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Buerger's Disease in England, there was no progression of the disease during a period of some years, despite the fact that she continued to smoke.[16] The physicians who reported her case stated that in their experience, "the disease continues in some well-established cases, despite the cessation of smoking and also goes into remission despite continuation of smoking."[17] Furthermore, in a 1988 paper on their retrospective study of 328 patients with Buerger's Disease, two Japanese researchers, Ohta and Shionoya, commented:

> [N]o progression of symptoms was observed in about one-half of the patients who continued smoking, and a few patients suffered from ischaemic ulcers even though they had abstained from tobacco.[18]

Other questions about the relationship between tobacco and Buerger's Disease also raise doubts about the causal hypothesis. For example, if tobacco causes Buerger's Disease, how does one explain the cases reported among nonsmokers, even in very young children?[19] Furthermore, how does one explain the differences seen over time in the ratio of male to female smokers with the disease?[20] In 1936, the ratio of women to men smokers in the United States was estimated at 1:6 while the ratio of women to men with Buerger's Disease was estimated at 1:70 to 1:500. In 1950, the ratio of women to men smokers fell to 1:4, yet there was "no proportionate increase" in the incidence of the disease among women

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smokers.[21] This suggests factors other than smoking must be involved.

Finally, some have claimed that since cigarette smoking has been related to Buerger's Disease, other forms of tobacco probably also play a role in the disease. However, a 1974 report on the results of a 20-year study of 25,000 snuff users and/or tobacco chewers in the state of Tennessee, where the use of these products is common, concluded that there was "no relationship between the use of unsmoked tobacco per se and intermittent claudication."[22] Intermittent claudication (pain in the foot or calf after exercise of the affected muscle) is one of the first symptoms noted by a patient with Buerger's Disease.[23]

Based on such observations, two British physicians, who describe Buerger's Disease as "a disease of unknown aetiology," concluded that the association between cigarette smoking and the disease "is not as clear as has been suggested in the past."[24]

Other Suspected Factors

Buerger's Disease is reportedly more common in the Orient, Eastern Europe and the Mediterranean than North America and, although "no explanation has ever been offered for this peculiar geographic distribution of disease,"[25] it suggests the possible

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involvement of genetic differences or environmental factors. A genetic influence is also suggested by the cases observed in nonsmokers and by the occasional familial occurrence of the disease reported in the literature.

Furthermore, a number of other suspects have been suggested as a cause of Buerger's Disease. These include fungal infections, socioeconomic class and/or occupation[26] and internal immune disorders.[27]

Conclusion

Despite claims regarding Buerger's Disease and the use of tobacco, the role of tobacco, if any, has not been determined. True Buerger's Disease is a relatively rare occurrence in relation to the world's population of smokers. Moreover, the issues of misdiagnosis, incidence rates, and other possible risk factors and reports that the disease progresses even after smoking is discontinued raise many questions about the hypothesis that tobacco causes Buerger's Disease.

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